7. Motterlini R, Foresti R. Biological signaling by carbon monoxide and carbon monoxide-releasing molecules. Am J Physiol Cell Physiol. 2017; 312(3): 302–313. https://doi.org/10.1152/ajpcell.00360.2016.
8. Queiroga CS, Almeida AS, Alves PM, Brenner C, Vieira HL Carbon monoxide prevents hepatic mitochondrial membrane permeabilization. BMC Cell Biol. 2011; 12: 1–8. https://doi.org/10.1186/1471-2121-12-10.
9. Qureshi OS, Zeb A, Akram M, Myung-Sic K, Kang J-H, Kim HS, Majid A, Han I, Chang SY, Bae ON, Kim JK. Enhanced acute anti-inflammatory effects of CORM-2-loaded nanoparticles via sustained carbon monoxide delivery. Eur J Pharm Biopharm. 2016; 108: 187–195. https://doi.org/10.1016/j.ejpb.2016.09.008.
10. Wei Y, Chen P, de Bruyn M, Zhang W, Bremer E, Helfrich W. Carbon monoxide-releasing molecule-2 (CORM-2) attenuates acute hepatic ischemia reperfusion injury in rats. BMC gastroenterol. 2010; 10: 42. https://doi.org/10.1186/1471-230X-10–42.
11. Wilson JL, Fayad Kobeissi S, Oudir S, Haas B, Michel B, Dubois Randé JL, Ollivier A, Martens T, Rivard M, Motterlini R, Foresti R. Design and synthesis of new hybrid molecules that activate the transcription factor Nrf2 and simultaneously release carbon monoxide. Chemistry. 2014; 20: 14698–14704. https://doi.org/10.1002/chem.201403901.
12. Yabluchanskiy A, Sawle P, Homer–Vanniasinkam S, Green CJ, Foresti R, Motterlini R. CORM-3, a carbon monoxide-releasing molecule, alters the inflammatory response and reduces brain damage in a rat model of hemorrhagic stroke. Crit Care Med. 2012; 40: 544–552. https://doi.org/10.1097/CCM.0b013e31822f0d64.

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EVALUATION OF SUSCEPTIBILITY OF REFERENCE STRAINS OF MICROORGANISMS TO THE COMBINED ACTION OF ESSENTIAL OILS AND MEXIDOL

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The susceptibility of the reference strains S. aureus ATCC 25923 and E. coli ATCC 25922 to 14 essential oils and their combinations with mexidol (ethylmethylhydroxypyridine succinate) was studied using the disk diffusion method. It was shown that a combination of all essential oils (with the exception of eucalyptus and ginger) with mexidol increases the susceptibility of S. aureus ATCC 25923 to these agents, with the most pronounced effect being observed with oils of lemon, lavender, fir, and rose. The susceptibility of E. coli ATCC 25922 to essential oils of cinnamon, mint, tea tree, rose, eucalyptus, cloves, and sage significantly increases when combined with mexidol, and this effect is the most pronounced when using combinations of mexidol with rose, eucalyptus, and clove oils. The discovered ability of mexidol to increase the susceptibility of microorganisms to essential oils can be a basis for the development of pharmaceutical compositions with these substances in which an enhanced antimicrobial effect will accompanied by an antioxidant activity and low toxicity.

Key words: microorganisms' susceptibility, *S. aureus*, *E. coli*, mexidol, essential oil.

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ОЦІНКА ЧУТЛИВОСТІ ЕТАЛОННИХ ШТАМІВ МІКРООРГАНІЗМІВ ДО КОМБІНОВАНОЇ ДІЇ ЕФІРНИХ ОЛІЙ І МЕКСИДОЛУ

Досліджено чутливість еталонних штамів мікроорганізмів *S. aureus* ATCC 25923 та *E. coli* ATCC 25922 до 14 ефірних олій та їх комбінацій з мексидолом (етилметилгідроксипіридину сукцинатом) за допомогою диск-дифузійного методу. Показано, що комбінування всіх ефірних олій (за винятком евкаліпту та імбиру) з мексидолом збільшує чутливість *S. aureus* ATCC 25923 до цих засобів, причому найбільш виразний ефект спостерігається стосовно олій лимону, лаванди, піхти та троянди. Чутливість *E. coli* ATCC 25922 ло ЕО кориці, м'яти, чайного дерева, рози, евкаліпту, гвоздики і шавлії істотно зростає при їх комбінуванні з мексидолом, причому найбільш виразним такий ефект є при використанні комбінацій мексидолу з оліями троянди, евкаліпту та гвоздики. Виявлена здатність мексидолу підвищувати чутливість мікроорганізмів до ефірних олій може стати основою для розробки фармацевтичних композицій з цими компонентами, в яких посилена антимікробна дія буде поєднуватись з антиоксидантною активністю і низькою токсичністю.

Ключові слова: чутливість мікроорганізмів, *S. aureus*, *E. coli*, мексидол, ефірна олія.

The study is a fragment of the research project "Study of the role of opportunistic and pathogenic infectious agents with different susceptibility to antimicrobial and antiviral drugs in human pathology", state registration No. 0118U004456.

Essential oils (EOs) are volatile secondary metabolites that give plants a characteristic aroma and taste. They are produced by more than 17,500 species of many plants families, but only about 300 of them are commercialized [15]. Having a content of two or three main components at the level 20–70 %, EOs are complex mixtures of terpenes, terpenoids and other compounds [15]. A known feature of EO is their antimicrobial action, which is characterized by a wide spectrum, is not attenuated at the presence of protein,

is not accompanied by toxic reactions, does not cause resistance, and is characterized by the influence on antibiotic-resistant strains of microorganisms [9, 15]. This is of particular interest in relation to the so-called crisis of antibiotic resistance, when the spread of antibiotic-resistant microorganisms precedes the development of new drugs against them [11]. Although the antimicrobial action of EOs has been sufficiently studied and described in numerous articles [5, 6, 7, 12], the real effect of EOs in vivo is much weaker as compared to synthetic compounds and antibiotics. Due to the volatile nature, high reactivity and oxidation with the formation of less active products and allergens, the effectiveness and duration of EOs action are limited [15]. Increasing the EOs antimicrobial activity can be achieved through the use of nanotechnology, combining them with each other, with antibiotics and adjuvants [8, 10, 14]. The role of antimicrobial adjuvant, as shown earlier, can be performed by mexidol (ethylmethylhydroxypyridine succinate), a synthetic antioxidant with antimicrobial properties [1], which is mostly positioned and used in clinic as a neurotropic agent [2].

The purpose of the work was to study the susceptibility of reference strains of microorganisms S. aureus ATCC 25923 and E. coli ATCC 25922 to combinations of EOs with mexidol.

Materials and methods. Determination of the susceptibility of microorganisms was carried out by the disk-diffusion method [4]. Reference strains of gram-positive microorganisms S. aureus ATCC 25923 and gram-negative microorganisms E. coli ATCC 25922, were obtained from the State Institution "Institute of Epidemiology and Infectious Diseases after L.V. Gromashevsky" NAMS of Ukraine (Kyiv). Their susceptibility to antibiotics was tested and corresponded to the etalon values [4]. To determine the susceptibility of microorganisms to mexidol, 20 % solution of substance of the drug (Bion, RF) was applied to 1000 μg/disk on empty sterile paper disks (HIMEDIA Laboratories Pvt Ltd, India). Disks were dried at room temperature and used as described [4]. In addition, 14 EOs and their combinations with mexidol were studied. For this purpose, EOs of cinnamon (Cinnamomum verum), lemon (Citrus limon), peppermint (Mentha piperita), tea tree (Melaleuca alternifolia) (all manufactured by LLC AROMA GROUP, Ukraine) as well as EOs of laurel (Laurus nobilis), ginger (Zingiber officinale), wormwood (Artemisia absinthium), calendula (Calendula officinalis), lavender (Lavandula officinalis), rose (Rosa damascena), eucalyptus (Eucalyptus globulus), cloves (Eugenia caryophyllata) and sage (Salvia officinalis) (all, starting with EO laurel, manufactured by LLC PTC Pharmacom, Ukraine) were applied on sterile empty disks and pre-prepared disks with mexidol (1000 μg/disk) immediately before placing them on the surface of Mueller-Hinton agar in Petri dishes with test cultures of microorganisms. The volume of every EO was 10 μl. Empty disks were used as a negative control. Standard disks with gentamicin (10 μg/disk) (Optimum System, Ukraine) served as a positive control. The susceptibility of microorganisms to the studied agents was evaluated by the growth inhibition zone greater than 10 mm. If the inhibition zone exceeded 25 mm, the microorganism was considered as highly susceptible; if such a zone was from 16 to 25 mm, microorganism was characterized as moderately susceptible; and if such a zone was from 10 to 16 mm – as minimally susceptible [3]. Inhibition zones were measured after 24 h of incubation at +37°C. Determination of the susceptibility of microorganisms was repeated 5 times, followed by statistical processing of the digital material using standard computer programs Statistica for Windows 8.0. The probability of the difference between the groups was assessed by Student's t-test. The difference was considered statistically significant at $p<0.05$.

Results of the study and their discussion. All the studied EOs caused inhibition of growth of the reference strain S. aureus ATCC 25923, however, the susceptibility of this test culture to EOs varied widely (table 1). Around the disks with EOs of cinnamon and ginger inhibition zones were greater than 25 mm, indicating the high susceptibility of the staphylococcus reference strain to these remedies. The inhibition zones from 16 to 25 mm were observed around disks with EOs of peppermint, tea tree, rose, clove and sage. Such results showed a moderate susceptibility of S. aureus ATCC 25923 to the mentioned agents. At the same time, this test culture was minimally susceptible to EOs of lemon, laurel, lavender, wormwood and calendula, for which the inhibition zones ranged between 10-16 mm. The inhibition zones around the disks with eucalyptus and fir EOs were less than 10 mm, indicating that the staphylococcus test culture was not susceptible to these oils.

The susceptibility of S. aureus ATCC 25923 to mexidol was moderate (table 1) in the absence of bacterial growth inhibition in the negative control and the characteristic values of inhibition zones in the positive control with gentamicin (23.0±0.2 mm). It was smaller than for EOs of cinnamon ($t=19.31$, $p<0.001$), cloves ($t=3.0$, $p<0.02$) and ginger ($t=7.80$, $p<0.001$); similar to the susceptibility to EOs of tea tree, rose and sage or higher than to EOs of lemon ($t=17.44$, $p<0.001$), peppermint ($t=2.77$, $p<0.05$), laurel ($t=3.25$, $p<0.02$), wormwood ($t=7.0$, $p<0.001$), lavender ($t=5.01$, $p<0.002$), calendula ($t=12.0$, $p<0.001$), eucalyptus ($t=30.5$, $p<0.001$) or fir ($t=24.5$, $p<0.001$).

The combination of EOs with mexidol increased inhibition of the growth of S. aureus ATCC 25923 (table 1).

Table 1

Zones of growth inhibition of the reference strain S. aureus ATCC 25923 under the influence of essential oils and their combinations with mexidol, M±m (n=5)

The name of essential oil or adjuvant	Diameter of the inhibition zone, mm	
	essential oil (10 μL/disk or mexidol (1000 μg/disk)	combination of essential oil with mexidol (10 μL+1000 μg/disk)
Mexidol (an adjuvant)	18.6±0.4	-
Cinnamon	39.4±1.0*	46.6±1.1*, #
Lemon	10.8±0.2*	30.2±0.6*, #
Peppermint	16.6±0.6*	23.4±0.2*, #
Tea tree	19.8±0.5	23.8±0.5*,#
Laurel	15.6±0.8*	21.4±1.0*, #
Ginger	27.0±1.4*	19.4±1.1 #
Wormwood	15.8±0.6*	23.0±0.6*, #
Calendula	13.8±0.5*	20.0±0.6*, #
Lavender	13.2±1.0*	25.0±0.9*, #
Rose	18.0±1.3	29.0±0.6*, #
Eucalyptus	6.4±0.4*	18.0±0.3 #
Cloves	19.8±0.9	24.0±0.6*, #
Fir	8.8±0.4*	21.2±1.1*, #
Sage	20.2±1.5	27.0±1.2*, #

Notes: In table 1 and the following: 1. The name of the essential oil is identified with a name of the plant from which it is obtained. 2. * – $p<0.05$ as compared to the zone of growth inhibition of the microorganism test culture around the disks with mexidol. 3. # – $p<0.05$ as compared to the zone of growth inhibition of the microorganism test culture around the disks with essential oil without mexidol.

In the samples of this group, except for the disks with EOs of ginger or eucalyptus and mexidol, the diameters of inhibition zones significantly exceeded those as compared to mexidol itself (t from 2.6 to 26.0, p less in the range of 0.02-0.001). Inhibition of staphylococcus test culture growth by combinations of EOs with mexidol also was more pronounced as compared to the corresponding oils. The growth inhibition zones of S. aureus ATCC 25923 when combining mexidol with EO cinnamon increased by an average by 7.2 mm ($t=4.84$, $p<0.002$), lemon – by 19.4 mm ($t=30.67$, $p<0.001$), peppermint – by 6.8 mm ($t=10.75$, $p<0.001$), tea tree – by 4 mm ($t=5.65$, $p<0.001$), laurel – by 5.8 mm ($t=4.53$, $p<0.002$) as compared to zones around the disks with the mentioned EOs themselves. Addition of mexidol provided an increase of growth inhibition zone for the EO of wormwood by 7.2 mm ($t=8.49$, $p<0.001$), calendula – by 6.2 mm ($t=7.94$, $p<0.02$), lavender – by 11.8 mm ($t=8.77$, $p<0.001$), rose – by 11 mm ($t=5.34$, $p<0.001$), eucalyptus – by 11.6 mm ($t=23.2$, $p<0.001$), cloves – by 4.2 mm ($t=3.88$, $p<0.005$), fir – by 12.8 mm ($t=10.59$, $p<0.001$), sage – by 6.8 mm ($t=3,54$, $p<0,005$) against analogical parameters for the EOs without adjuvant. Only in the case of the combination of ginger EO with mexidol, inhibition of staphylococcal test culture growth was less than with a single application of this oil by 7.6 mm ($t=4.27$, $p<0.005$). As can be seen, in all cases of combining EOs with mexidol, except the combinations of ginger and eucalyptus oils with this drug, inhibition zones of staphylococcus test culture probably differed in the direction of increase from those around the disks with each of the components of the composition. This indicated that a combined effect of the two agents on the microorganism was observed and proved the ability of mexidol to increase the susceptibility of the reference strain S. aureus ATCC 25923 to EOs. The most pronounced effect was when using combinations with lemon, lavender, fir and rose oils.

The susceptibility of the test culture E. coli ATCC 25922 to EOs varied widely, as well as the susceptibility of the reference strain S. aureus ATCC 25923, but to none of the studied oils was not high (table 2). Inhibition zones from 16 to 25 mm were formed around the disks with EOs of cinnamon and tea tree that has shown a moderate susceptibility to them of the reference strain of escherichia. The test culture of E. coli ATCC 25922 was minimally susceptible to EOs of peppermint, calendula, rose, cloves and sage, when the inhibition zones were 10-16 mm. Inhibition zones around the disks with the rest of EO were less than 10 mm that confirmed the lack of susceptibility of the reference strain of the intestinal rod to these agents.

E. coli ATCC 25922 had moderate susceptibility to mexidol in the absence of inhibition of bacterial growth in the negative control and typical for this strain values of inhibition zones in the positive control on gentamicin (21.0±0.2 mm). The susceptibility of the E. coli reference strain to mexidol was lower than to cinnamon EO ($t=14.14$, $p<0.001$) and in all other cases – higher than to EOs, in particular to lemon oil ($t=40.75$, $p<0.001$), peppermint ($t=11.67$, $p<0.001$), tea tree ($t=6.0$, $p<0.002$), laurel ($t=13.79$, $p<0.001$), ginger ($t=40.75$, $p<0.001$), rose ($t=2.02$, $p<0.001$), wormwood ($t=21.47$, $p<0.001$), lavender ($t=40.75$, $p<0.001$), calendula ($t=4.47$, $p<0.005$), eucalyptus ($t=12.49$, $p<0.001$), cloves ($t=4.21$, $p<0.005$), sage ($t=5.62$, $p<0.001$) and fir ($t=17.44$, $p<0.001$).

Comparing the susceptibility of the reference strains of staphylococcus and Escherichia to individual EOs, it could be noted that S. aureus ATCC 25923 is more susceptible to them than E. coli

ATCC 25922. After all, 10 studied oils effectively inhibited the development of the first test culture, and the second – by 5 of 14 investigated samples of EOs.

The combination of EOs with mexidol increased the inhibition zones of E. coli test culture (table 2).

Table 2

Zones of growth inhibition of the reference strain E. coli ATCC 25922 under the influence of essential oils and their combinations with mexidol, M±m (n=5)

The name of essential oil or adjuvant	Diameter of the inhibition zone, mm	
	essential oil (10 μL/disk) or mexidol (1000 μg/disk)	combination of essential oil with mexidol (10 μL+1000 μg/disk)
Mexidol (an adjuvant)	17.0±0.4	-
Cinnamon	25.0±0.4*	30.8±0.7*, #
Lemon	0*	17.0±0.4 #
Peppermint	10.4±0.4*	14.2±0.7*, #
Tea tree	20.0±0.3*	22.4±0.5*, #
Laurel	9.2±0.4*	18.8±1.0*,#
Ginger	0*	17.2±0.5 #
Wormwood	7.4±0.2*	20.2±1.4 #
Calendula	12.6±0.9*	17.8±1.9 #
Lavender	0*	19.4±1.0 #
Rose	10.2±0.4*	22.4±1.0*, #
Eucalyptus	9.4±0.5*	20.6±0.9*, #
Cloves	13.6±0.7*	25.4±0.2*, #
Fir	9.2±0.2*	17.2±0.7#
Sage	13.4±0.5*	24.0±0.5*, #

In the samples of this group, except for combinations of the adjuvant and EOs of lemon, ginger, wormwood, calendula, lavender or fir, the size of inhibition zones significantly exceeded those formed by mexidol alone (t from 3.47 to 18.78, p less than 0.02-0.001). Inhibition of growth E. coli ATCC 25922 test culture by all combinations of EOs with mexidol was more pronounced as compared to the corresponding oils. In particular, the inhibition zones of the reference strain of E. coli from the combined action of mexidol with EO cinnamon increased by an average of 5.8 mm ($t=7.19$, $p<0.001$), lemon – by 17 mm ($t=17.88$, $p<0.001$), peppermint – by 4.2 mm ($t=4.71$, $p<0.002$), tea tree – by 2.4 mm ($t=3.75$, $p<0.01$), laurel – by 9.6 mm ($t=8.91$, $p<0.001$), ginger – by 17.2 mm ($t=15.73$, $p<0.001$), wormwood – by 12.8 mm ($t=9.05$, $p<0.001$) , calendula – 5.2 mm ($t=2.47$, $p<0.05$), lavender – 19.4 mm ($t=13.68$, $p<0.001$), rose – 12.4 mm ($t=11.33$, $p<0.001$), eucalyptus – by 11.2 mm ($t=11.27$, $p<0.001$), cloves – by 11.8 mm ($t=16.21$, $p<0.001$), fir – by 8 mm ($t=10.99$, $p<0.001$) and sage – by 10.6 mm ($t=14.99$, $p<0.001$) against relevant parameters of EOs without adjuvant. However, only for the compositions of EO cinnamon, peppermint, tea tree, rose, eucalyptus, cloves and sage inhibition zones probably differed from those with a separate application of both mexidol and the corresponding oil. This excluded the possibility of taking the effect of mexidol itself for the combined action of drugs and indicated the ability of this agent to increase the sensitivity of the reference E. coli strain to the EOs. The most pronounced effect was when using combinations of mexidol with rose, eucalyptus and clove oils.

Analyzing the obtained results, it should be noted that, although test cultures S. aureus ATCC 25923 and E. coli ATCC 25922 are widely used in the study of antimicrobial properties of EOs, the data on their inhibition zones in the disk-diffusion method have different values for oils from the same plant determined in the different researches [5, 6, 7, 12, 15] and there are no single etalon indicators. This is due to the peculiarities of the preparation of disks with EOs and certain differences in the ratio of chemical components of the each oil depending on the method of production, region and conditions of cultivation and collection of medicinal raw materials [15]. Obviously, therefore, in some cases, the susceptibility of the reference strains of microorganisms determined by us differed from that given in the articles of other authors. For example, the susceptibility of the reference strain of staphylococcus in our experiments was higher to the corresponding data of cinnamon EO and lower to lemon EO than indicated [5, 12].

In this experiment, the susceptibility of both reference strains of bacteria to mexidol was quite pronounced, although lower than in our previous studies [1] that may be due to the use of paper disks from another manufacturer with a slightly different degree of diffusion of the active substances in agar.

It is also noteworthy that the susceptibility of gram-positive cocci to EOs in general was greater than the sensitivity of gram-negative rods, as described by other authors, explaining this phenomenon by the difference in cell wall structure of these categories of bacteria and the presence of lipoproteins and lipopolysaccharides in the external membrane of gram-negative microorganisms that prevents the penetration of lipophilic compounds into the bacterial cell [6].

The combination of EOs with mexidol almost naturally increased the susceptibility of the reference strains of staphylococcus and escherichia to these drugs, which was similar to the ability of mexidol to increase the susceptibility of mentioned microorganisms to antibiotics [1]. Because the adjuvant effect of mexidol has affected many oils with different chemical compositions, it is difficult to relate it to a particular class of compounds (monoterpenes, terpenoids, terpenoid oxides, etc.) that determine the mechanism of action of EOs. Taking into account the ability of mexidol to change the viscosity of cell membranes and regulate the functioning of membrane-bound complexes in the macroorganism [2], we can assume that it facilitates the distribution of EOs in lipid components of the cell wall and lipids of the cell membrane of bacteria, in such a way increasing microorganism's susceptibility to volatile oils which are believed to be membrane-tropic agents that cause bactericidal action by disrupting the integrity of bacterial cell membranes and electrolyte leakage [7].

A single case where the combination of ginger EO with mexidol reduced the susceptibility of the test culture of S. aureus against such EO itself, can be regarded as antagonism of components similar to those described in mixtures of EOs, one of which has high antimicrobial activity [13].

The revealed ability of mexidol to increase the susceptibility of microorganisms to EOs can be the basis for the development of pharmaceutical compositions with these components, primarily for external use, in which enhanced antimicrobial action will develop while maintaining antioxidant activity and low toxicity.

Conclusions

1. Reference strain S. aureus ATCC 25923 shows high susceptibility to EOs of cinnamon and ginger, moderate susceptibility to EOs of peppermint, tea tree, rose, cloves and sage, minimal susceptibility to EOs of lemon, laurel, lavender, wormwood and calendula in the absence of such to EOs of eucalyptus and fir, and also shows moderate susceptibility to mexidol.

2. The reference strain of E. coli ATCC 25922 has a moderate susceptibility to EOs of cinnamon and tea tree, minimal susceptibility to EOs of peppermint, calendula, rose, cloves and sage in the absence of significant susceptibility to EOs of lemon, laurel, ginger, wormwood, lavender, eucalyptus, or fir, and displays a moderate susceptibility to mexidol.

3. The combination of EOs (excluding eucalyptus and ginger EOs) with mexidol increases the susceptibility of S. aureus ATCC 25923 to these agents, with the most pronounced effect being observed for lemon, lavender, fir and rose oils.

4. The susceptibility of E. coli ATCC 25922 to EOs of cinnamon, peppermint, tea tree, rose, eucalyptus, cloves and sage increases significantly, when the oils are combined with mexidol, and the most pronounced effect is when using combinations of mexidol with the oils of rose, eucalyptus and cloves.

References

1. Vazhnichaya EM, Bobrova NA, Devyatkina TA, Loban GA, Devyatkina NN. Vliyanie emoksipina i meksidola na razvitie kultur etalonnyih shtammov mikroorganizmov i ih chuvstvitelnost k antibIotikam. Eksp Klin Farmakol. 2019;2:16-20. doi:10.30906/0869-2092-2019-82-2-16-20. [In Russian]

2. Voronina TA, Ivanova EA. Kombinirovannoe primenenie meksidola s izvestnyimi lekarstvennyimi sredstvami. Zh Nevrol Psihiatr im. S.S. Korsakova. 2019;119(4):115-24. doi: 10.17116/jnevro2019119041115. [In Russian]

3. Dikiy IL, Sidorchuk II, Holupyak IYu, Sheveleva NE Mikrobiologiya: Rukovodstvo k laboratornyim zanyatiyam: Uchebnoe posobie dlya studentov farmatsevticheskih VUZov i farmatsevticheskih fakultetov meditsinskih institutov. Kiev: ID «Professional»; 2004. 594 s. [In Russian]

4. Semina SA, Sidorenko SV, Rezvan SP, Grudinina SA, Strachunskiy LS, Stetsyuk OU i dr. Opredelenie chuvstvitelnosti mikroorganizmov k antibakterialnyim preparatam (Metodicheskie ukazaniya MUK 4.2.1890-04). Klin mikrobiol antimikrob himioter. [Internet] 2004 [tsitirovano 2019 Dek. 26];6(4):306-59. Dostupno: https://cmac-journal.ru/en/publication/2004/4/cmac-2004-t06-n4-p306/cmac-2004-t06-n4-p306.pdf [In Russian]

5. Abers M, Schroeder S, Goelz L, Sulser A, St. Rose T, Puchalski K, Langland J. Antimicrobial activity of the volatile substances from essential oils. BMC Complement Med Ther. 2021 Apr 17;21:124. doi:10.1186/s12906-021-03285-3.

6. Bachir RG, Benali M. Antibacterial activity of the essential oils from the leaves of Eucalyptus globulus against Escherichia coli and Staphylococcus aureus. Asian Pac J Trop Biomed. 2012 Sep; 2(9):739–42. doi: 10.1016/S2221-1691(12)60220-2.

7. Chouhan S, Sharma K, Guleria S. Antimicrobial activity of some essential oils – present status and future perspectives. Medicines (Basel). 2017 Aug 8;4(3):58. doi: 10.3390/medicines4030058.

8. Fadil M, Fikri-Benbrahim K, Rachiq, S, Ihssane B, Lebrazi S, Chraibi M et al. Combined treatment of Thymus vulgaris L., Rosmarinus officinalis L. and Myrtus communis L. essential oils against Salmonella typhimurium: Optimization of antibacterial activity by mixture design methodology. Eur. J. Pharm. Biopharm. 2018 May, 126, 211–20. doi: 10.1016/j.ejpb.2017.06.002.

9. Kon KV. Rai MK. Plant essential oils and their constituents in coping with multidrug-resistant bacteria. Expert Rev Anti-Infect Ther. 2012 Jul;10(7):775-90. doi: 10.1586/eri.12.57.

10. Langeveld WT, Veldhuizen EJ, Burt SA. Synergy between essential oil components and antibiotics: a review. Crit Rev Microbiol. 2014 Feb;40(1):76-94. doi: 10.3109/1040841X.2013.763219.

11. Michael CA, Dominey-Howes D, Labbate M. The antibiotic resistance crisis: causes, consequences, and management. Front Public Health. 2014 Sep 16;2:145. doi: 10.3389/fpubh.2014.00145

12. Nabavi SF, Di Lorenzo A , Izadi M, Sobarzo-Sánchez E, Daglia M, Nabavi SM. Antibacterial effects of cinnamon: from farm to food, cosmetic and pharmaceutical industries. Nutrients. 2015 Sep;7(9):7729–48. doi: 10.3390/nu/7095359.

13. Semeniuc CA, Pop CR, Rotar AM. Antibacterial activity and interactions of plant essential oil combinations against Gram-positive and Gram-negative bacteria. J. Food Drug Anal. 2017 Apr, 25(2), 403–8. doi: 10.1016/j.jfda.2016.06.002.
14. Sotelo-Boyás M, Correa-Pacheco Z, Bautista-Baños S, Gómez Y. Release study and inhibitory activity of thyme essential oil-loaded chitosan nanoparticles and nanocapsules against foodborne bacteria. Int J Biol Macromol. 2017 Oct;103:409-14. doi: 10.1016/j.ijbiomac.2017.05.063.
15. Wińska K, Mączka W, Łyczko J, Grabarczyk M, Czubaszek A, Szumny A. Essential oils as antimicrobial agents – myth or real alternative? Molecules. 2019 Jun 5,24(11): 2130. doi: 10.3390/molecules24112130.

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RESULTS OF RESEARCH THE MINERAL CONTENS OF THE BLOOD AND THE ORAL FLUID IN PREGNANT WOMEN SUFFERING FROM PERIODONTITIS AND IRON DEFICIENCY

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Pregnancy due to its physiological course is supported by intensification of all kinds of intechanges including both macroelement and trace element ones. Metal imbalance is closely connected to the activity of some enzymes, vitamins and metallobiotics (iron, magnesium, cuprum and zink). The violation of the microelements' interchange, which have a huge bioactivity is connected with the impact on metabolism, sanguification, tissue respiration, determines its vital role in pathogenesis of many illnesses including periodontitis. As a result, providing mineral homeostasis is more special and complicated during pregnancy, especially one that is affected by iron deficiency. The research of serum mineral interchange proved that imbalance of trace elements (microelementosis) is essential component of iron deficiency, pathogenesis in pregnant women and it strengthens according to the development of generalized periodontitis. Iron and cuprum biometals deficiency, especially important during pregnancy, turned to be particularly keen. We have observed the gradual decrease of the content of biometals in serum in both groups of the survey with the development of generalized periodontitis. So, iron deficiency anemia leads to disorders of mineral homeostasis of oral fluid and blood serum, and the progression of generalized periodontitis increases the deficiency of trace elements in the these biological fluids.

Keywords: pregnant women, iron deficiency, generalized periodontitis, trace elements, blood, oral fluid.

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РЕЗУЛЬТАТИ ДОСЛІДЖЕННЯ МІНЕРАЛЬНОГО СКЛАДУ КРОВІ ТА РОТОВОЇ РІДИНИ ВАГІТНИХ ЖІНОК, ХВОРИХ НА ГЕНЕРАЛІЗОВАНИЙ ПАРОДОНТИТ, НА ТЛІ ЗАЛІЗОДЕФІЦИТНОЇ АНЕМІЇ

Вагітність, навіть за умов її фізіологічного перебігу, супроводжується посиленням усіх видів обміну, в тому числі і макро- та мікроелементного. Дисбаланс металів тісно пов'язаний з активністю деяких ензимів, вітамінів і металобіотиків (залізо, магній, мідь, цинк). Порушення метаболізму мікроелементів, висока біологічна активність яких пов'язана з впливом на обмін речовин, процеси кровотворення, тканинного дихання, визначають їх важливу роль у патогенезі низки захворювань, у тому числі і пародонтиту. У зв'язку з цим, забезпечення мінерального гомеостазу набуває особливого значення у період вагітності, особливо ускладненої залізодефіцитною анемією. Метою нашого дослідження стало вивчення мінерального та мікроелементного складу крові та ротової рідини вагітних жінок із залізодефіцитною анемією, хворих на генералізований пародонтит в залежності від ступеня важкості пародонтиту. Дослідження мінерального складу сироватки крові вагітних жінок довело, що дисбаланс мікроелементів (мікроелементоз) є важливим компонентом патогенезу залізодефіцитної анемії у вагітних, та посилюється з розвитком генералізованого пародонтиту. Отже, залізодефіцитна анемія призводить до порушень мінерального гомеостазу сироватки крові та ротової рідини, а прогресування генералізованого пародонтиту підсилює дефіцит мікроелементів у цих біологічних рідинах.

Ключові слова: вагітні жінки, залізодефіцитна анемія, генералізований пародонтит, мікроелементи, кров, ротова рідина.

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The vast majority of scientists are interested in the task of both saving the health of mother and a child and the study of the oral cavity condition during the pregnancy aiming to warn the onset of dental chronic disease. The study of dental diseases in pregnant women suffering from somatic pathology still remains topical [13].